

REMARKS

Status of the claims

Claims 57, 68-71, 87-91, 93 and 96-102 were pending. As shown above, claim 57 has been amended to specify that the non-naturally occurring zinc finger protein binds to a region of cellular chromatin that is sensitive to DNaseI digestion. See, e.g., Examples 2 and 5 of the as-filed specification. Withdrawn claim 91 has been similarly amended and withdrawn claim 93 canceled, without prejudice or disclaimer. In addition, claim 57 has also been amended to make explicit that the non-naturally occurring zinc finger protein includes 3 or more zinc finger domains and that at least one of the zinc finger domains comprises a non-naturally occurring recognition helix. See, e.g., page 27 of the as-filed specification. Inasmuch as withdrawn claims 91, 93, and 96-102 contain all of the limitations of the elected composition claims, they are eligible for rejoinder upon allowance of the claims under consideration.

Rejections Withdrawn

Various obvious-type double patenting rejections and rejections under 35 U.S.C. § 102 over U.S. Patent Nos. 7,026,467 and 7,163,824 have been withdrawn.

Obviousness-type double patenting

The second Advisory Action again reiterated the rejection of the examined claims under the judicially created doctrine of obviousness-type double patenting over U.S. Patent Nos. 6,919,204 and 6,824,978. (Advisory Action, page 2).

Applicants reiterate that the claims of these patents do not render obvious the pending claims and are therefore not conflicting. Nonetheless, to expedite prosecution, submitted herewith is a Terminal Disclaimer over the cited patents. Applicants direct the Examiner's attention to § 802.04 of the MPEP where it is clearly stated that the filing of a terminal disclaimer is not an admission that the rejection is proper:

The filing of a terminal disclaimer to obviate a rejection based on nonstatutory double patenting is not an admission of the propriety of the rejection. *Quad Envi-ronmental Technologies Corp. v. Union Sanitary*

District, 946 F.2d 870, 20 USPQ2d 1392 (Fed. Cir. 1991). The court indicated that the "filing of a terminal disclaimer simply serves the statutory function of removing the rejection of double patenting, and raises neither a presumption nor estoppel on the merits of the rejection."

Thus, the rejections have been obviated, the withdrawn claims should be rejoined and examined and all claims proceed to allowance.

35 U.S.C. § 102

The second Advisory Action also reiterated the rejections based on the same patents cited above for double-patenting. (Advisory Action, page 2). In addition, claims 57, 68, 70 and 71 remained rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Shin et al. (1999) *Proc. Nat'l Acad. Sci. USA* 96:2880-2884 (hereinafter "Shin") and claims 57, 68 and 69 remained rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Stacey et al. (1999) *Plant Cell* 11:349-363 (hereinafter "Stacey").

To the extent that the foregoing amendments do not obviate the rejections, Applicants traverse.

The pending claims are drawn to complexes comprising non-naturally occurring zinc finger proteins that include at least one non-naturally occurring recognition helix. By contrast, Shin and Stacey fail to disclose zinc finger proteins with designed and/or selected recognition helix. Instead, Shin discloses "truncation mutations of the GLI3 zinc finger transcription factor." See, Abstract of Shin. Stacey also fails to disclose any zinc finger proteins as claimed, as none of their "mutants" contain a non-naturally occurring recognition helix. See, Figures 1 and 6 of Stacey.

Furthermore, Shin, Stacey and U.S. Patent Nos. 7,235,354; 7,177,766; 7,045,304; 6,989,269; 6,785,613; 6,780,590; 6,777,185; 6,599,692; and 6,453,242 are all silent as to complexes in which the zinc finger proteins are necessarily and inevitably bound to a region of cellular chromatin that is sensitive to a DNaseI digestion.

In view of the foregoing amendments, the Examiner's lengthy remarks regarding the alleged "true" definition of an "accessible" region are not germane to the pending claims. The only issue is whether any of the above references expressly or inherently teach a complex as claimed. As repeatedly noted throughout prosecution, anticipation

requires that every limitation of the claim at issue must appear identically in a single reference. *In re Bond*, 910 F.2d 831, 832, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). Furthermore inherent anticipation cannot be established by probabilities or possibilities (see, *Continental Can Co. USA, Inc. v. Monsanto Co.*, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991):

Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.

Thus, in the instant case, the burden is on the Examiner to show that the cited references teach cells in which the engineered zinc finger protein is necessarily and inevitably bound to DNaseI hypersensitive sites.

Shin, Stacey and U.S. Patent Nos. 7,235,354; 7,177,766; 7,045,304; 6,989,269; 6,785,613; 6,780,590; 6,777,185; 6,599,692 are all silent as to DNaseI sensitivity. Thus, these references do not expressly anticipate the pending claims.

Furthermore, as continually noted, none of the cited references inherently (necessarily and inevitably) teach that zinc finger proteins are bound to DNaseI hypersensitive sites. In fact, the evidence of record teaches that zinc finger proteins are functional when bound to regions that are not sensitive to digestion with DNaseI. See, Zhang et al. (Ref. C5 of IDS filed August 22, 2006 and considered November 10, 2006), showing that engineered zinc finger proteins have been shown to form complexes with non-DNaseI sensitive regions of cellular chromatin (see, e.g., Figure 6 and page 33857, paragraph bridging left and right columns, emphasis added).

In order to further test this idea, we performed a DNaseI hypersensitivity analysis of the promoter region. We did not detect preferred sites of cleavage in the vicinity of 862, nor were any sites detectable within 3 kilobase pairs between 460 and 3673 5' of the EPO transcription unit (Fig. 6, A and B...This result leads to the observation that the EPOZFP862a, -b, and -c proteins are not gaining access through a preexisting DNase I-hypersensitive site in chromatin.

In addition, as previously noted, Wong et al. (1997) (Exhibit A of Response filed July 6, 2005 and Ref C4 of IDS filed August 22, 2006 and considered November 10, 2006) and Cirillo et al. (1998) (Exhibit B of Response filed July 6, 2005 and Ref C1 of IDS filed August 22, 2006 and considered November 10, 2006) establish that naturally occurring transcription factors also do not necessarily bind to DNaseI sensitive regions of cellular chromatin.

Thus, it has not been shown to be inherent in these references that any engineered zinc finger protein will necessarily and inevitably be bound to a DNaseI-sensitive region of cellular chromatin, as claimed.

CONCLUSION

For the reasons set forth herein, allowance of the claims under consideration, and rejoinder and allowance of the withdrawn claims, are requested.

Respectfully submitted,

Date: September 10, 2008

By: _____



Dahna S. Pasternak

Registration No. 41,411

Attorney for Applicants

ROBINS & PASTERNAK LLP
1731 Embarcadero Road, Suite 230
Palo Alto, CA 94303
Telephone: (650) 493-3400
Facsimile: (650) 493-3440